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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,183	08/18/2004	Masahiko Negishi	4239-64458-02	2375

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EXAMINER	
SHAFER, SHULAMITH H	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/505,183	NEGISHI ET AL.	
	Examiner	Art Unit	
	Shulamith H. Shafer, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 August 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/18/04,2/22/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims

Election/Restriction:

Applicants' election (communication of 10 October 2006, in response to requirement for restriction of 14 September 2006), of Group I, claims 1-17, drawn to drawn to polypeptide sequence of a mutated nuclear orphan receptor, a kit comprising said polypeptide and a composition comprising said polypeptide is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants have cancelled claims 18-35. Claims 1-17 are pending in the instant application.

Objections

Information Disclosure Statement

The information disclosure statement filed 18 August 2004 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. The first reference AG on page 1 is lined through and has not been considered because the reference to a sequence is presented without identification of a database and the date sequence was deposited. Appropriate correction is required.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Rejections

35 U.S.C. § 101:

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-14 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 1 is directed to a polypeptide comprising a mutated receptor. Claim 1, as written does not sufficiently distinguish over a mutated polypeptide that naturally exists in cells because the claims do not particularly point out any non-naturally occurring differences between the claimed sequences and naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. (See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of language indicating an "isolated" polypeptide (See MPEP 2105).

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "A polypeptide encoding a non-constitutively active....receptor". It is unclear how a polypeptide could encode another polypeptide. Furthermore, the claim recites "a non-constitutively active nuclear orphan receptor comprising a mutation....., wherein the mutation renders the polypeptide less constitutively active". It

is unclear how a non-constitutively active receptor can be made less constitutively active. The claim is vague and indefinite in reciting a "less constitutively active" in such a way as to make this a relative term. The term is not defined by the claim, the specification does not provide standard definitions, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Furthermore, the claim is vague and indefinite in reciting the term "native". It is unclear what applicant intends by this term; it is unclear if applicant intends wild-type protein. If applicant intends any and all naturally occurring sequences, such could be found not only indefinite, but also to lack written description. Additionally, the claim identifies the protein as "CAR". "CAR" is identified as proteins of several different activities in references submitted on the IDS of 22 February 2005 and 18 August 2004. Roelvink et al. (1999. Science 286:1568, cited on IDS of 22 February 2005) identifies CAR as Coxsackie adenovirus receptor; Ueda et al (2002. Mol Pharm 61:1284-1288, cited on IDS of 18 August 2004) identify the CAR as constitutive androstane receptor; Ueda et al (2002. Mol Pharm 61:1-6, cited on IDS of 18 August 2004) identify the protein as nuclear orphan constitutive active receptor. While the name itself may have some notion of the activity of the protein, there is nothing in the claim that distinctly identifies the protein. Others in the field may isolate the same protein and give it an entirely different name or give the same name to a different protein. Applicant should particularly point out definitive characteristics associated with the protein. Describing biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly identify what the protein is. Thus, "CAR" is not sufficient to identify the protein of the claimed invention, one of skill in the art would not be able to determine what molecules are encompassed.

Claims 1 and 9 are vague and indefinite for reciting "less constitutively active" (Claim 1) and "substantially decrease the non-constitutive activity" (Claim 9). A constitutively active receptor protein is one that continuously signals, even in the absence of a cognate ligand. It is unclear how a receptor can be "more" or "less" constitutively active.

Claims 2-8 are vague and indefinite in reciting amino acid positions without presenting a reference sequence. The claims do not present any accession number,

database, or reference date for the recited sequences. Therefore, the recitation of amino acid residue positions is meaningless.

Claim 2 is vague and indefinite for reciting "the mutation corresponds to murine CAR (mCAR) position.....and/or hCAR position Leu343". It is unclear how the mutation could be a mutation at more than one residue position (the use of the conjunction "and").

Claim 4 is vague and indefinite for reciting "wherein the mutation corresponds to mCAR position Thr176 and mCAR position Leu352". It is unclear how the mutation could be a mutation at more than one residue position.

Claim 6 is vague and indefinite for reciting "wherein the mutation corresponds to hCAR position Leu342 and hCAR position Leu343". It is unclear how the mutation could be a mutation at more than one residue position.

Claims 10 and 13 are vague and indefinite in reciting "confers". It is unclear how a polypeptide may confer a property to another polypeptide.

Claim 16 is rejected under 35 U.S.C. 112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 22 is considered indefinite because a kit, by definition, must contain 2 or more elements and the interrelationships between the elements must be explicitly stated (see In re Venezia 530 F.2d 956 CCPA 1975).

Claims 11, 12, 14, 15 and 17 are included in this rejection as dependent upon rejected claims.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working samples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention: The invention is drawn to mutated CAR receptors, said mutation rendering the receptors "less constitutively active".

The claims are broadly drawn to a mutated CAR protein comprising a mutation that renders the receptor non-constitutively active, that is responsive to xenochemicals and/or steroids. The claims recite mutations at specific amino acid residues; however, no reference sequences are recited in the claims.

The specification discloses:

With respect to CAR receptor activity:

Direct activation of CAR in response to various drugs, such as phenobarbitol (PB) has been observed *in vivo*. CAR is active even in the absence of agonistic

chemicals in a cell-based transfection assay *in vitro*, [paragraph 0005, PGPUB 20050107590, the publication of the instant application].

With respect to CAR:

The term "CAR" includes any CAR gene, cDNA, RNA, or protein from any organism, that has the property of being constitutively active *in vitro* and/or the ability *in vivo* to be inducible by a CAR-responsive steroid, such as estrogen, and/or the ability *in vivo* to be inducible by a CAR-responsive xenochemical, such as phenobarbital (PB) and TCPOBP [paragraph 0030]. CAR includes mammalian CAR sequences, such as mouse CAR (mCAR, for example Genbank Accession Nos. AF009327 and AAC53349) and human CAR (hCAR, for example Genbank Accession Nos. U90716 and AAC51234). A CAR sequence includes a full-length wild-type (or native) sequence, as well as CAR allelic variants, variants, fragments, homologs or fusion sequences that retain the ability to be constitutively active *in vitro* [paragraph 0031]. Thus, the wild-type CAR protein is not specifically defined. The accession numbers disclosed are disclosed only as examples; they do not provide a clear identification of the sequence of the protein of interest, since no dates of deposit are indicated. Information in databases is constantly being changed and updated. Without an indication of the date of deposit, one would be unable to determine the exact reference sequence of the wild-type receptor.

With respect to non-CAR:

The disclosure teaches that a non-CAR protein is a protein comprising a mutation in the wild-type CAR sequence which is a less constitutively active than the wild-type protein when tested in an *in vitro* assay system but retains the ability to be induced by CAR-responsive xenochemicals and steroids [paragraph 0033]. The non-CAR sequences include variants, fragments, and fusions thereof that retain desired properties, such as responsiveness to xenochemicals and estrogens [paragraph 0076]. However, without a specific reference sequence, one would not be able to determine whether mutations at specific residue sites would produce the required protein, a protein with less constitutive activity, much less determine which variants, fragments etc. would retain said activity.

Working examples: The working examples teach production of expression vectors by cloning an entire mCAR (GenBank Accession NoLAR009327) or hCAR (GenBank Accession No:Z30425) coding sequences (Example 1). However, these sequences are not unambiguously identified, as the dates of the deposits are not stated. Example 6 teaches that a single mutation of Thr176 (in mCAR sequence) to valine or leucine decreased the constitutive activity of mCAR. Example 7 teaches that an Ala substitution of Leu 352 in mCAR decreased constitutive activity; an Ala substitution of Leu 342 of hCAR, as well as the double mutation L342A/L343A decreased hCAR constitutive activity. However, none of the working examples unambiguously identify the reference sequences of the mCAR or hCAR polypeptide.

The art teaches: the term CAR is applied to proteins of different functions. Roelvink et al. (1999. Science 286:1568, cited on IDS of 22 February 2005, abstract) identifies CAR as Coxsackie adenovirus receptor; Ueda et al (2002. Mol Pharm 61:1284-1288, cited on IDS of 18 August 2004, abstract) identify the CAR as constitutive androstane receptor; Ueda et al (2002. Mol Pharm 61:1-6, cited on IDS of 18 August 2004, abstract) identify the protein as nuclear orphan constitutive active receptor. Without unambiguous identification of a reference sequence, one could not determine what specific proteins (CAR or non-CAR) the claims of the instant invention are drawn to.

Therefore, based on the discussions above concerning the art's recognition of a number of different functional proteins named CAR, the teachings in the specification that the non-CAR sequences include variants, fragments, and fusions and the lack of any unambiguous reference sequence recited in the claims or disclosed in the specification, the skilled artisan would be unable to predict that producing mutations at the indicated amino acid residues would result in a protein with the functional characteristics of the protein of the instant invention.

Due to the large quantity of experimentation necessary to determine which amino acid residues one must mutate to produce a protein with less constitutive activity, the lack of direction/guidance presented in the specification regarding same as no reference sequences are unambiguously disclosed, the absence of sufficient working examples

directed to same, the complex nature of the invention, the state of the prior art establishing that the term CAR may identify a number of functional diverse proteins, and the breadth of the claims which fail to recite a reference sequence, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Claims 1, 9-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptides comprising a mutation in the **native** CAR sequences. The specification envisions the term encompassing all mammalian CAR sequences, including full-length wild-type sequences, as well as CAR allelic variants, variants, fragments, homologs or fusion sequences that retain the ability to be constitutively active in vitro and/or the ability to activate a PB enhancer element in the presence of PB in vivo. In certain examples, CAR will have at least 80% sequence identity, for example 85%, 90%, 95%, or 98% sequence identity to a native CAR [paragraph 0031]. However, no "native sequences" are unambiguously recited. The specification teaches two exemplary sequences, mouse CAR (mCAR, for example Genbank Accession Nos. AF009327 and AAC53349) and human CAR (hCAR, for example Genbank Accession Nos. U90716 and AAC51234); however, even these exemplary sequences do not provide a clear identification of the sequence of the protein of interest, since no dates of deposit are indicated. Additionally, none of the working examples unambiguously identify the reference sequences of the mCAR or hCAR polypeptide. Thus, the claims are drawn to an entire genus of molecules, identified as "native" or wildtype sequences, none of which are unambiguously identified.

Additionally, the claims are drawn to polypeptides that have mutations at specified amino acid residues. These mutations result in changing a protein which is constitutively active *in vitro* to one that is activated by xenobiotics or steroid hormones.

The claims do not disclose any specific reference sequence, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of proteins that is defined only by functional parameters.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of mutated amino acids and functional characteristics to be assayed. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more that a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directe to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, the full breadth of the claims does not meet the written description provision of 35 U.S.C. 112, first paragraph, since no specific reference sequence is unambiguously identified. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6, 8-14, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Tomko et al. (1997. PNAS 94:3352-3356). Tomko et al. teach a sequence of a CAR receptor; the receptor has a mutation at position 176 (Glu substituted for Thr at the indicated residue, has mutations corresponding to hCAR position Leu342 and hCAR position Leu343, wherein the mutation is Leu342 to Ala342. The polypeptide has proline substituted for leucine at position 343, a conservative amino acid substitution, since both are nonpolar, hydrophobic residues (see Figure 1 and enclosed alignment). The claims do not identify a reference sequence; therefore, absent evidence to the contrary, the sequence taught by Tomko et al. meets the limitations of the claims. Tomko et al teach Western blot assays (page 3353, 1st column, 2nd paragraph); the cell lysates used in such assays constitute a composition comprising the CAR polypeptide. While Tomko et al. do not explicitly teach a polypeptide wherein the polypeptide confers xenochemical metabolizing activity to a xenochemical-metabolizing enzyme, wherein the xenochemical metabolizing enzyme metabolized a xenochimical from the group consisting of phenobarbital or TCPOBOP,

or wherein the polypeptide confers steroid metabolizing activity to a steroid metabolizing enzyme wherein the steroid-metabolizing enzyme metabolizes a steroid selected from the group consisting of estrogen and estradiol, case law has established that the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Also, case law has established that a compound and all of its properties are inseparable, as are its processes and yields (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). Thus, the teachings of Tomko et al anticipate all the limitations of claims 1-3, 6, 8-14, and 17.

Claims 1, 10-14, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawamoto et al. (2000. Mol Endoc 14:1897-1905, cited on IDS of 18 August 2004). The reference teaches a nuclear receptor, CAR, whose ability to transactivate the NR1 response element found in the *CYP2B* gene increases upon incubation with estradiol and TCPOBOP (abstract and page 1899, Figure 1). Kawamoto et al. do not identify the receptor as a mutated receptor. However, claim 1, the independent claim of the instant invention, does not recite a specific reference sequence; one would be unable to determine a sequence comprising the "native" (wild-type) protein. Since one is unable to determine exactly what the reference sequence is, one cannot determine what a mutated sequence would comprise. The claim identifies the mutated receptor by a functional parameter: as one that is "less constitutively active" than the "native" (interpreted as wild-type) sequence. The term "less constitutively active" is vague and indefinite (see above discussion) and is herein interpreted to mean that the receptor can be activated by a ligand. Kawamoto et al. teach estradiol and TCPOBOP increase luciferase activity in cells transfected with an NR1-tk-luciferase plasmid, in the presence of mCAR expression plasmid. A receptor that can be activated by a ligand is interpreted to be one that is "less constitutively active". Thus, the protein taught by Kawamoto meet the limitations of claim 1. Since the NR1 response element is found in a gene coding for an enzyme that is key to metabolizing steroids and xenobiotics, the

Cyp2b10 gene, absent evidence to the contrary, the luciferase assay is detecting xenochemical and/or steroid metabolizing activity *in vitro*. Cell lysates (page 1905, 1st column, 2nd paragraph) constitute a composition comprising the CAR polypeptide. Thus, the teachings of Kawamoto et al anticipate all the limitations of claims 1, 10-14, and 17.

Claims 1, 10-12, and 15-17 are rejected under 35 U.S.C. 102(a) as being anticipated by Tzammell et al. (2000. Mol. Cell Biol. 20:2951-2958). Tzammell et al. teach a nuclear receptor, CAR, whose ability to transactivate the CYP promoter elements is increased in the presence of TCPOBOP, thus demonstrating that TCPOBOP is an agonist ligand for CAR (abstract). Tzammell et al. does not teach the nuclear receptor as a mutation of the native sequence. However, as discussed above, claim 1, the independent claim of the instant invention, does not recite a specific reference (wild-type) sequence; since one is unable to determine exactly what the reference sequence comprises, one cannot determine what a mutated sequence would comprise. The claim identifies the receptor by a functional parameter: as one that is "less constitutively active" than the "native" (interpreted as wild-type) sequence. The term "less constitutively active" is vague and indefinite (see above discussion, under 112, 2nd rejections) and is herein interpreted to mean that the receptor can be activated by a ligand. The reference teaches that CAR transactivation (a measure of CAR activity) is increased in the presence of TCPOBOP, a member of the Phenobarbital-like class of CYP-inducing agent. Thus, a receptor which can be activated by a ligand would meet the limitations of claim 1. The reference teaches a method of assaying *in vitro* interactions comprising an incubation mixture of [^{35}S]methionine labeled CAR or CARdm in the presence of TCPOBOP, thereby anticipating the limitations of claims 15-17. Thus the teachings of Tzammell et al. anticipate all the limitations of claims 1, 10-12 and 15-17.

Conclusion:

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shulamith H. Shafer, Ph.D. whose telephone number is 571-272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SHS

Lorraine Spector

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